REMARKS

Status of the claims

Claims 1-4 are pending in the application with claims 3 and 4 being withdrawn. Claim 1 is amended herein. Claim 1 has been amended to delete the explicit recitation of the feature that the LAK-induced sample is prepared by treating the lymphocyte fractions with the extract of *Lentinus edodes* mycelium in the absence of IL-2 and to incorporate the subject matter of claim 2. Claim 2 has been cancelled.

Statement of the substance of the interview

Applicants' would like to thank the Examiner and her supervisor for the interview conducted on January 3, 2007. During the interview the Applicants discussed with the examiners the rejections under 35 U.S.C.§112, 1st paragraph and 35 U.S.C.§102.

The issues that were discussed will be presented in more detail under each rejection heading below.

Rejections under 35 U.S.C.§112, 1st paragraph

The Examiner has rejected claims 1 and 2 under 35 U.S.C.§112, 1st paragraph with the assertion that the limitation "in the absence of IL-2" is not supported by the specification. The Examiner asserts that "[t]he instant disclosure does not provide evidence that the screening material comprising Lentinus edodes mycelium does not contain IL-2 or does not induce IL-2 expression in the test condition." Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The specification indicates in several locations that the instant *Lentinus edodes* extract induces LAK activity in the absence of IL-2. For example, page 6, lines 14-15 states, "We also found that said extract can be used as an alternative to IL-2 to induce LAK activity in vitro."

Similarly, page 10, lines 21-26 state, "Screening methods using screening materials of the present invention can be performed according to the method of Takagi et al. with the exception that a screening material such as the extract of *Lentinus edodes* mycelium of the present invention is used in place of IL-2". Finally, it is clear from the experimental description found on pages 18-19 of the specification that IL-2 is not present when the extract of the invention is used to induce LAK activity. Thus, contrary to the assertion of the Examiner, the specification fully support the recitation of the feature that "in the absence of IL-2".

This issue was discussed at the interview and a consensus is believed to have been reached that explicit recitation of "in the absence of IL-2" is not necessary to render the invention as claimed patentable. As such, in the interest of facilitating the allowance of the claims and because this feature is inherent to the composition used in the method of claim 1, the feature has been deleted from claim 1.

Rejections under 35 U.S.C.§102(b)

Arinaga et al. - Claim 1 has been rejected under 35 U.S.C.§102(b) as being anticipated by Arinaga et al. The Examiner asserts that Arinaga et al. teach the *in vitro* enhancement of LAK by lentinan and that the LAK activity of isolated NK cells from patients is enhanced after lentinan administration. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The Examiner's assertion that Arinaga et al. teach the *in vitro* enhancement of LAK by lentinan and that the LAK activity of isolated NK cells from patients is enhanced after lentinan administration is technically incorrect. A full consideration of the reference shows that any increased LAK activity reported in Arinaga et al. is actually an enhancement of IL-2 induced LAK activity rather than directed stimulation of LAK cells by the lentinan.

As noted, the Examiner asserts that Arinaga et al. disclose an *in vitro* method of determining enhancing LAK activity by lentinan. This issue was discussed in depth at the interview. As Applicants' representative pointed out in the interview, in Arinaga et al. LAK activity is only seen with the *in vitro* treatment of lymphocytes with IL-2 (see, for example, Abstract, "Preparation of effector cells" on Page 536, and the last sentence of "Discussion" on page 538). Moreover, Arinaga et al. simply describe that lentinan is administered to patients *in vivo*. Arinaga et al. make neither mention nor discussion of lymphocytes being treated with lentinan *in vitro*. As such, the present invention, which is drawn to a method for determining whether an extract of *Lentinus edodes* mycelium *in vitro* has a LAK activity-enhancing effect, is not anticipated by the disclosure of Arinaga et al. Applicants understanding from the interview is that the examiners concurred upon further review of the reference that Arinaga et al. only administers the extract *in vivo* and subsequently looks at the activity *in vitro,* i.e. there is no *in vitro* exposure of the LAK cells to the extract. As such, Arinaga et al. should be withdrawn as a reference against the presently claimed invention.

In addition, as described above with regard to the rejection under 35 U.S.C.§112, 1st paragraph, the extract of *Lentinus edodes* mycelium of the present invention is entirely different from lentinan, as described in Arinaga et al. Thus, the extracts used in the instantly claimed method and that of Arinaga et al., respectively, are completely different in composition. Claim 1 has been amended to incorporate the subject matter of claim 2, which defines the process by which the extract is made, and which results in an extract that is different from that of Arinaga et al. As such, the present invention is further distinguished from Arinaga et al. by the feature of the extract used in the method. As such, withdrawal of the rejection is respectfully requested.

Yamamoto et al. – The Examiner has rejected claims 1 and 2 as being anticipated by Yamamoto et al. Applicants strongly traverse this rejection and withdrawal thereof is respectfully requested.

As stated in MPEP §707.07(g) "Piecemeal examination should be avoided as much as possible." It appears to Applicants that the rejection over Yamamoto et al. is a perfect example of a form of "piecemeal" examination because Applicants have twice addressed and overcome rejections of claims 1 and 2 based on this same reference during the examination of the instant application. As such, Applicants question the reliance on this reference yet a third time, this time in support of a rejection for anticipation under 35 U.S.C.§102(b).

In the interest of facilitating the allowance of the claims, claim 1 has been amended by incorporating the subject matter of claim 2, thereby defining the method by which the extract is made. The amendment of Claim 1 further distinguishes the instant invention over the disclosure of Yamamoto et al. by defining the extract used in the recited method. The process used in amended claim 1 to make the extract results in an extract that is different from that of Yamamoto et al.

The extract of *Lentinus* edodes mycelium as made according to the process recited in claim 1 contains 39.4 % of glucose as a primary component and has sugar composition of Xyl 15.2 %, Ara 8.2 %, Man 8.4 %, Gul 39.4 %, Gal 5.4 %, GlcN 12.0 %, GluUA 11.3 % (see, Example 1 of the present specification). On the other hand, Yamamoto et al. describes that the composition of sugars of the extract of the reference "was 70 % of xylose, 20 % of arabinose, and 8 % of glucose (data not shown)" (see page 1910, right column, second paragraph).

Comparing the sugar composition of the extract of the present invention and that of Yamamoto et al., there are at least the following differences between the extract of the present invention and that of Yamamoto et al., as disclosed in the instant specification and the disclosure of Yamamoto et al.

	Xylose	Arabinose	glucose
the present invention	15.2 %	8.2 %	39.4 %
Yamamoto et al.	70%	20%	8%

As is clear from the comparison above, the sugar composition of the extract of the present invention is completely different from that of Yamamoto et al.

In addition, as described in Example 1 (see pages 13-14 of the present specification) the extract of the present invention contains "25.3 % (w/w) carbohydrates", "19.7 % (w/w) proteins" and "2.6 % (w/w) polyphenols" and "further contains 8 % crude fat, 22 % crude ash and about 20 % soluble nitrogen-free materials other than carbohydrates". On the other hand, the LEM and JLS-18 in Yamamoto et al. contain the following components:

Table II. Chemical composition of LEM and JLS-18 of Yamamoto et al.

%	Lignin	Sugar	Protein	Ash	Other
LEM	27.4	33.9	10.4	13.5	14.8
J LS-18	76.4	21.3	2.3	N.D.	-

The differences between the components of the extract of the present invention and the components of the preparations of Yamamoto et al. are summarized in the following table.

%	Lignin	Sugar	Protein	Ash	Other
LEM of Yamamoto et al.	27.4	33.9	10.4	13.5	14.8
J LS-18	76.4	21.3	2.3	N.D.	-
the present invention	-	25.3	19.7	22	30.6

Thus, the extract of the present invention, as made in accordance with the process recited in claim 1, is a different composition than that in Yamamoto et al. in the profile of the sugars present, as well as at least the protein and ash content. Thus, a comparison of the specification and the disclosure of Yamamoto et al. shows that the extract of the present invention is definitely different from that of Yamamoto et al. As such, the instant invention is both novel and unobvious over the disclosure of Yamamoto et al.

Due to the differences between the components of the extract of *Lentinus edodes* mycelium of the present invention and the extract of Yamamoto et al. as described above, those ordinarily skilled in the art could not have predicted whether the extract of *Lentinus edodes* mycelium of the present invention would exhibit a LAK activity enhancing effect, based on the disclosure of Yamamoto et al.

In addition, the present invention possesses unexpected advantages that make the invention unobvious over the teachings of Yamamoto et al. The present invention is directed to a method for determining whether the extract has a LAK activity enhancing effect before administration of the extract to a patient, based on the correlation between the activity of the extract *in vitro* with that *in vivo.* In Yamamoto et al., on the other hand, the extracts are disclosed as being an immunopotentiating agent useful for treating type B chronic hepatitis and for having immunopotentiating activity, such as antiviral activity, respectively.

Yamamoto et al. only discloses that the extract of the reference has an effect on activating NK cells, T cells and macrophages, and does not contain any description as to whether the extract enhances LAK activity. On the other hand, the present application clearly discloses for the first time that the extract of the invention can enhance LAK activity both *in vivo* and *in vitro,* and that the *in vitro* function of the extract correlates with that *in vivo*. Such differences in effects between the present invention and that of Yamamoto et al. are due to the differences between the components of the extract of the present invention and that of Yamamoto et al. Therefore, the present invention is therefore both novel and unobvious over Yamamoto et al. and withdrawal of the rejection is respectfully requested.

In view of the above amendments and remarks, Applicants believe the pending application is in condition for allowance. Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD, Reg. No. 40, 069 at the telephone number of the undersigned

below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.14; particularly, extension of time fees.

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Respectfully submitted,

By _____

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